

# **Sero-conversion rate and its predictors among HIV discordant couples at Jimma University Specialized Hospital**

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**A thesis to be submitted to Jimma University, College of Public Health and Medical Sciences, Department of Internal Medicine for partial fulfillment of the requirements for specialty certificate in Internal Medicine.**

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## Abstract

**Background:** All HIV-1 transmissions occur from an infected to an uninfected partner, but sub-Saharan Africa is unique in that a high proportion of HIV-1 transmissions may occur in stable, long-term partnerships, in which one member is HIV-1-infected. Although this has been reported from other countries, there is no study done in Ethiopia on sero-conversion rate and its predictors in HIV discordant couples.

**Objectives:** To assess the incidence of and risk factors for HIV acquisition in a cohort of HIV-uninfected partners from HIV discordant couples in Jimma University Specialized Hospital (JUSH) Anti Retroviral Treatment (ART) clinic.

**Methods:** A retrospective cohort study was conducted at ART clinic and VCT center of Jimma University Specialized Hospital (JUSH) from November 16/2013 to February 15/2014 on 322 sero-discordant couples that are selected from the registered clients in the period from 2003 to 2013 in JUSH Voluntary Counseling and Testing (VCT) center. A structured questioner was used to collect data on socio-demographic characteristics, duration since the participants knew their HIV serostatus, social and behavioral characteristics and clinical and immunological characteristics. HIV-uninfected adults living in HIV discordant couple relationships were counseled and tested for HIV. The data was collected by medical resident physicians working at the ART clinic of the hospital. Data was cleaned, edited and entered to SPSS version 16.0 computer software for analysis. The survival analysis and determination of risk factors for HIV acquisition was done using Cox regression model. The value of  $p < 0.05$  was considered statistically significant.

**Results:** The overall HIV incidence rate was 1.7; and 1.8 and 1.6 per 100 PYO in men and women respectively. In the follow-up risk analysis, Late WHO stage at enrollment was predictive of a reduced risk of HIV acquisition [Stage II, (adjusted risk ratio [aRR] = 0.2, 95% confidence interval [CI]=0.06-0.83); Stage III (aRR = 0.03, 95% CI = 0.04-0.27)] and no seroconversion occurred in HIV-uninfected partners whose partners were in WHO clinical stage IV.. There were no seroconversions among participants who reported consistent condom use during the study.

**Conclusion:** Our study found a low rate of HIV transmission among serodiscordant couples in the study area, but it contributes to a clinically significant population that mandates implementation of preventive strategy. Antiretroviral Therapy programs should be combined with HIV prevention interventions that emphasize always using condoms.

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## List of Acronyms/Abbreviations

<b>AIDS</b>	Acquired Immunodeficiency Syndrome
<b>ART</b>	Antiretroviral Therapy
<b>CD4</b>	Cluster of Differentiation 4
<b>CHCT</b>	Couples HIV voluntary Counseling and Testing
<b>EDHS</b>	Ethiopia Demographic and Health Survey
<b>GUDs</b>	Genital Ulcer Diseases
<b>HIV</b>	Human Immunodeficiency Virus
<b>HSV</b>	Herpes Simplex Virus
<b>JUSH</b>	Jimma University Specialized Hospital
<b>NNRTI</b>	Non nucleoside reverse transcriptase
<b>NRTI</b>	Nucleoside Reverse Transcriptase Inhibitors
<b>OIs</b>	Opportunistic Infections
<b>PCP</b>	Pneumocystis Carinii Pneumonia
<b>PCR</b>	Polymerase Chain Reaction
<b>PGL</b>	Persistent Generalized Lymphadenopathy
<b>PI</b>	Protease Inhibitors
<b>PLWHA</b>	People Living With HIV/AIDS
<b>PYO</b>	Person-Years of Observation
<b>RNA</b>	Ribonucleic Acid
<b>SPSS</b>	Statistical Package for Social Sciences
<b>STDs</b>	Sexually transmitted diseases
<b>UNAIDS</b>	United Nations Programme on HIV/AIDS
<b>VCT</b>	Voluntary Counseling and Testing
<b>WHO</b>	World Health Organization

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## Chapter One: Introduction

### 1.1: Back Ground

Acquired Immune Deficiency Syndrome (AIDS) is caused by the Human Immunodeficiency Virus (HIV). Since the original description in 1981 of unusual cluster of cases of PCP (Pneumocystis Carinii Pneumonia) and Kaposi Sarcoma in previously healthy homosexual males, substantial advances in our understanding of AIDS have been achieved. The identification of a cytopathic retrovirus in 1983 and development of a diagnostic serologic test for HIV-1 in 1985 have served as the basis for developing improvement in diagnosis (1). In Ethiopia the first two cases of HIV infection were reported in 1984 (2).

HIV is a retrovirus that results in progressive destruction of the immune system, especially CD4+T-lymphocytes. It weakens the immune system, making the body susceptible to secondary and Opportunistic Infections (OIs) (1).

HIV is transmitted person-to-person from sexual contact, by transfusion of infected blood products, from women to their infants either in utero, intrapartum, or via breast milk, or by percutaneous injection with contaminated needles or other devices. Direct blood-to-blood contact such as occurs with blood transfusion, venous puncture with a hollow-bore needle containing infected blood, or significant mucosal disruption during sexual activities, and carries the highest risk. A number of biological factors are also associated with the risk of transmission, including size of the infectious inoculum, higher HIV viral load in the index case, genital ulcer disease in either the index case or recipient, mucosal abrasions or trauma and possibly, immune activation in the recipient(1).

World Health Organization (WHO) classifies HIV-infected patients based clinical signs and symptoms. Around two-third of patients develop “flue-like ”symptoms in the first three weeks following the infection (Primary HIV Syndrome). After this phase, the virus goes to clinical latency (but not viral latency) in the majority of adult patients. Patients in the first stage present with Persistent Generalized Lymphadenopathy (PGL) or otherwise are asymptomatic. The occurrence of minor muco-cutaneous manifestations marks the onset of WHO clinical stage II. More deep infections and some recurrent infections will put the patient to clinical stage III. Presence of AIDS defining OIs and/or malignancies is called Stage IV conditions. Patients with CD4+ cell count <200/mm<sup>3</sup> are labeled as AIDS regardless of their clinical stage (27).

Standard laboratory diagnosis rests on antibody tests to the virus as well as detection of the viral antigen in the blood polymerase chain reaction (PCR).Whereas, the treatment relies on a combination of powerful antiretroviral drugs to reduce the viral load which includes: Nucleoside/Nucleotide reverse transcriptase inhibitors (NRTIs/NtRTIs), Non Nucleoside reverse transcriptase inhibitors (NNRTIs), Protease inhibitors (PIs), Integrase inhibitors, Fusion inhibitors and Entry inhibitors (1).

The term sero-discordant is generally used to describe people of different HIV antibody status in stable marriage relationships and a sero-discordant or discordant couple is “a couple where one partner is HIV positive and the other is HIV negative” (3).

In some relationships, discordance exists from the onset, but in other cases, sero-discordance emerges from within an already established and known sero-concordant negative relationship as a result of one partner becoming newly infected with HIV or receiving a diagnosis of HIV infection acquired before the relationship. The nature of the relationship defining a couple is not uniformly defined; it can be a casual relationship, a stable relationship either formally married or informal marriages (4).

## 1.2: Statement of the Problem

The transmission of HIV through heterosexual sex has been one of the primary drivers of the AIDS epidemic world-wide. Sero-discordant couples have been used to study heterosexual transmission risk because of the high frequency of sexual acts that occur in stable relationships.

Since its detection in 1981 HIV has taken millions of people's lives. As a result individuals, families and societies have been enormously affected by the consequence of the virus. The sero-discordance phenomenon is one scenario of the virus which is currently controversial and mysterious.

The HIV pandemic remains a global health challenge. According to the 2012 United Nations Joint Program on AIDS (UNAIDS) report on the global AIDS epidemic, globally, 34.0 million [31.4 million–35.9 million] people were living with HIV at the end of 2011 and Sub-Saharan Africa remains most severely affected, with nearly 1 in every 20 adults (4.9%) living with HIV and accounting for 69% of the people living with HIV worldwide (6).

The number of people acquiring HIV infection in 2011 was 2.5 million [2.2 million–2.8 million] and sub-Saharan Africa accounted for 71% of the incidence (6).

The HIV/AIDS situation of Ethiopia has evolved from two cases in 1984; to more than two million people living with HIV/AIDS (PLWHA) currently. The HIV prevalence among adults age 15-49 in the 2011 Ethiopia Demographic and Health Survey (EDHS) is 1.5 % (2).

The percentages of couples in HIV sero-discordant relationships range from 5 to 31% in the various countries of Africa (7). In a study conducted at five sub-Saharan HIV affected countries (Tanzania, Kenya, Burkina Faso, Cameroon & Ghana), at least two thirds of the infected couples are discordant couples. Between 30 and 40 % of the infected couples are couples where the female partner only is infected (3).

In the 2011 Ethiopia Demographic and Health Survey(EDHS),more than 6,000 cohabiting couples were tested for HIV and among these 1.7% were HIV positive; of these HIV positive couples more than 65% reportedly were sero-discordant (in 63 % of couples the female partner is HIV positive and the male partner is HIV negative)(2).

In a case–control study conducted at VCT center of JUSH in all registered sero-discordant couples and sero-concordant couples that were selected from the registered clients in the period from 2003 to 2010, the prevalence of sero-discordance in the study population (i.e. South East Ethiopia) was found to be 8.4% (8).

The sero-discordant status will have serious impact especially when it is occurring among married couples because it requires couples to make serious decisions. Sero- discordant couples face the challenge of making a decision either to continue living together or not, as well as the decision about whether to have children. Sexual practice issues, especially with the practice of safer sex, bearing the responsibility of preventing the virus transmission to the uninfected partner are also a concern for such couples. Furthermore, as one of the partners is the only one living with HIV, he/she will need access to care and treatment, ideally with the support of their HIV negative partner .This will require the decision and commitment of both partners to live together and help each other despite the difference in their HIV status(4).

Individuals in HIV discordant relationships are one of the major high risk groups contributing to a new incidence of HIV in Sub-Saharan Africa (9). With the absence of HIV cure and a vaccine, behavior practices such as condom use and abstinence are key strategies in prevention of HIV. HIV prevention programs among discordant couples are traditionally based on three types of interventions: (1) Couples HIV Voluntary Counseling and Testing (CHCT), via both community-based outreach and in antenatal clinics, (2) Group-based workshops with sero-discordant couples, and (3) Integrated Antiretroviral Therapy and HIV prevention programs. These programs often include risk reduction counseling, referrals to treatment, counseling on family planning, and an avenue to further care and support services (4).

Studies have shown that the annual HIV incident rate of HIV negative partners in discordance sero converting reaches as high as 20% higher than their counterparts in HIV concordant negative couples (10). If unchecked, this may result in increased morbidity and a strain on the national health expenditures, reduced production and thus, poverty. Socially this may result in marriage breakups and increased number of orphans.

Studying HIV-1-discordant couples may contribute to understanding correlates of HIV-1 immunity and acute infection. Additionally, HIV-1-discordant couples are an important population for prevention efforts and currently, HIV-1-discordant couples are increasingly taken as a valuable source of participants for HIV vaccine and prevention trials (5).

The high prevalence of sero-discordance in Ethiopia calls for special attention to couples living under such conditions (2). But there are only few research studies done, focusing only on the prevalence of sero-discordance while none have been researched on the sero-conversion rate and its predictors among HIV discordant couples in Ethiopia and in the study area. The paucity of high quality studies and knowledge concerning these aspects signifies the need for further study in this area.

## **Chapter Two: Literature Review**

### **2.1: Literature Review**

#### **2.1.1: Overview**

Misconceptions about discordance are wide spread among couples and counselors. Common explanations includes: the concept of a hidden infection not detectable by HIV tests, belief in immunity and the thought that gentle sex protected HIV-negative partners. Such explanations for discordance reinforce denial of HIV risk for the negative partner within discordant couples and potentially increase transmission risk (11).

#### **2.1.2: HIV Incidence in Sero-discordant Couples**

On a retrospective cohort study done in Zhumadian city, Henan province, China on 1,927 sero-discordant couples over 3 years, there were 84(4.4%) sero-conversions on a total follow-up time of 4918 person-years (median 2.84 years) and the incidence rate was 1.71 per 100 PYO(12).

A nested matched case–control study within a larger cohort of 2135 south Indian discordant couples included 70 cases (3.3%) that sero-converted during 12 months study follow-up period and 167 matched controls who remained persistently sero-discordant. The incidence of HIV infection among the initially sero-negative partners was 6.52 per 100 PYO (13).

The impact of addressing couples on the HIV epidemic can never be over emphasized particularly in Sub-Saharan Africa where UNAIDS estimates over 63% of new infections to be acquired from stable relationships (6). Studies have shown that transmission rate in Sub-Saharan Africa stable discordant couples can be as low as 1.9 per 100 PYO to as high as 19.0 per 100 PYO (5).

495 HIV-uninfected adults living in HIV discordant couple relationships were enrolled from HIV discordant couples enrolled in an HIV vaccine trial feasibility study and followed for 2 years in Masaka, Uganda. Of the 495 initially HIV-uninfected adults 34 seroconverted during 786.6 PYO and the overall HIV incidence rate was 4.3 per 100 PYO (14).

#### **2.1.3: Predictors of Sero-conversion among Sero-Discordant Couples**

##### **Socio-demographic Factors:**

Most of the studies following-up HIV-negative or sero-discordant couples in countries facing generalised HIV epidemics tended to show that women are specifically at high risk of HIV infection within their regular partnership, presumably due to the infidelity of men and an increased biological susceptibility for women. Previous studies in Masaka, Uganda (15) and Mwanza, Tanzania (10), found that HIV incidence in women with HIV-infected spouses was twice that of men. But recent studies show no significant difference in HIV incidence between men and women (14, 16).

## **Clinical and Immunological Factors:**

### **1. CD4 T lymphocyte count of HIV Infected Partner**

A study from Western India documented a lower incidence rate of sero-conversion (1.22 per 100 PYO) among sero-discordant couples with high CD4 T lymphocyte counts (17).

In a prospective study of 3400 heterosexual HIV-1 sero-discordant couples from 7 African countries, the rate of HIV-1 transmission from HIV-1 infected partners not receiving ART was highest for those with CD4 counts <200 cells/mm<sup>3</sup> (8.79 per 100 PYO), and was relatively similar across higher CD4 count strata: 2.79, 1.70, and 1.82 per 100 PYO for CD4 counts 200–349, 350–499, and ≥500 cells/mm<sup>3</sup>, respectively, and there was no statistically significant difference in these rates (p=0.09). In this study no HIV-1 transmissions were seen among couples in which the HIV-1 infected partner initiated ART at a CD4 count <200 cells/ mm<sup>3</sup> (18).

In contrary the study in china reported that, there was no statistical difference in the median CD4 counts and after stratification into three groups based upon last recorded CD4 count level (>350, 200–349, 0–199 cells/μL), between those index cases who transmitted HIV to their spouses and those index partners who did not transmit HIV(16).

### **2. WHO Stage of the HIV Infected Partner**

On a similar study in China, there were 73 sero-conversions among the 1,656 sero-discordant couples that had a spouse with a clinical diagnosis of AIDS and among the 271 couples that had a HIV-positive spouse without AIDS, there were 11 sero-conversions. The result showed there was no statistical difference between these sero-conversion rates (p = 0.79) (16).

The likelihood of HIV transmission is not constant but varies over disease course, primarily in accordance with plasma viral load. In retrospectively identified 235 monogamous, HIV-discordant couples in a Ugandan population-based cohort study, after sero-conversion of the index partner, the rate of transmission within the first 2.5 months was almost 12-fold higher than that observed in prevalent index couples (19).

### **3. ART use by HIV Infected Partner**

ART dramatically improves the health and survival of HIV-1-infected individuals and also significantly reduces their infectiousness and likelihood of transmitting HIV-1 to partners. In the Masaka, Uganda study, ART initiated according to the national HIV treatment guidelines was associated with a reduced risk of heterosexual HIV acquisition [6.0 per 100 PYO among participants whose HIV-infected partners were ART naïve, compared to 1.1 per 100 PYO among those whose partners were receiving ART, an 82% difference (14)]. Similarly, the magnitude of ART effect on HIV-1 transmission risk was greatest for persons with CD4 counts <200 cells/mm<sup>3</sup>, emphasizing the potential synergy of ART for clinical and prevention benefits in persons whose CD4 counts have fallen to 200 cells/ mm<sup>3</sup> (18).

#### **4. Sexually Transmitted Infections**

Treatable Genital Ulcer Diseases (GUDs) are common and important correlates of HIV transmission within discordant heterosexual couples (21). Sexually transmitted diseases (STDs) that cause breach of the mucosal surfaces facilitate HIV transmission across the genital/gut mucosae. A study that analyzed data from a prospective study of Partners in Prevention Herpes simplex virus (HSV)/HIV Transmission Study in African HIV-1–serodiscordant couples found an independent 2.65-fold increased risk of infection associated with GUD by self-report or exam in HIV-1–uninfected partners (22).

##### **Social and Behavioral Factors:**

###### **1. Alcohol Use**

Alcohol use before sexual intercourse has been associated with increased risk of HIV acquisition in discordant couple. This is attributed to alcohol related disinhibition that results in increased risk behaviors such as non-use of condoms (20). In the Masaka, Uganda study, a baseline history of alcohol use was associated with a nearly three-fold increase in the risk of HIV acquisition (14). Similarly, the study in South Indian discordant couples one-third of patients (index cases) who transmitted HIV to their spouse between 6 and 12 months of care consumed alcohol on a regular basis, which was higher than patients in persistently discordant relationships (13).

###### **2. Extramarital Sex Partners**

Risk-reduction measures adopted by the HIV-negative partner should be taken into account when counseling sero-discordant couples. A prospective study was conducted to measure the sexual behaviors of HIV-negative individuals in sero-discordant couples. Data was from the Partners in Prevention HSV/HIV Transmission study that was carried out from 2004 to 2008 in seven African countries. A total of 3,381 sero-discordant couples were enrolled in the study. Over the two years of follow-up, the number of outside partners among the uninfected individuals in the couple increased from 3.1 % to 13.9 %. There was also an increase of the uninfected partner reporting no sexual activity with the infected partner and an increase of sexual activity with an outside partner during the follow-up period.

Condom use was more common among outside partners than with the HIV-positive partner. Of those who HIV seroconverted during the study and reported to have an outside partner, most (86 %) had an HIV subtype that was distinct from their HIV-positive partner, which indicates that they did not acquire HIV from their primary relationship (23).

###### **3. Condom Use**

Male condom-promotion interventions increase condom use and are the cornerstone of HIV prevention. In addition correct and consistent use of condoms is a highly effective tool for HIV-1 prevention. For prevention of HIV infection, STDs, re-infections and maintaining stability of families, discordant couples are encouraged to use condoms during sexual encounters. Analyses from the Partners in Prevention HSV/HIV Transmission Study found that male condoms were associated with 79% lower risk of HIV-1 transmission on a per- contact basis (24).



A prospective study followed 60 HIV discordant couples for an average of 2.2 years in Kigali, the capital of Rwanda, with the outcome of interest "Condom use in the couple and HIV sero-conversion in the negative partners". During follow up two of the 23 HIV negative men and six of the 30 HIV negative women seroconverted (sero-conversion rates of 4 and 9 per 100 PYO). Condom use was less common among those who seroconverted (100% v 5%,  $p=0.01$  in men; 67% v 25%,  $p=0.14$  in women) (25).

## **2.2: Significance of the Study**

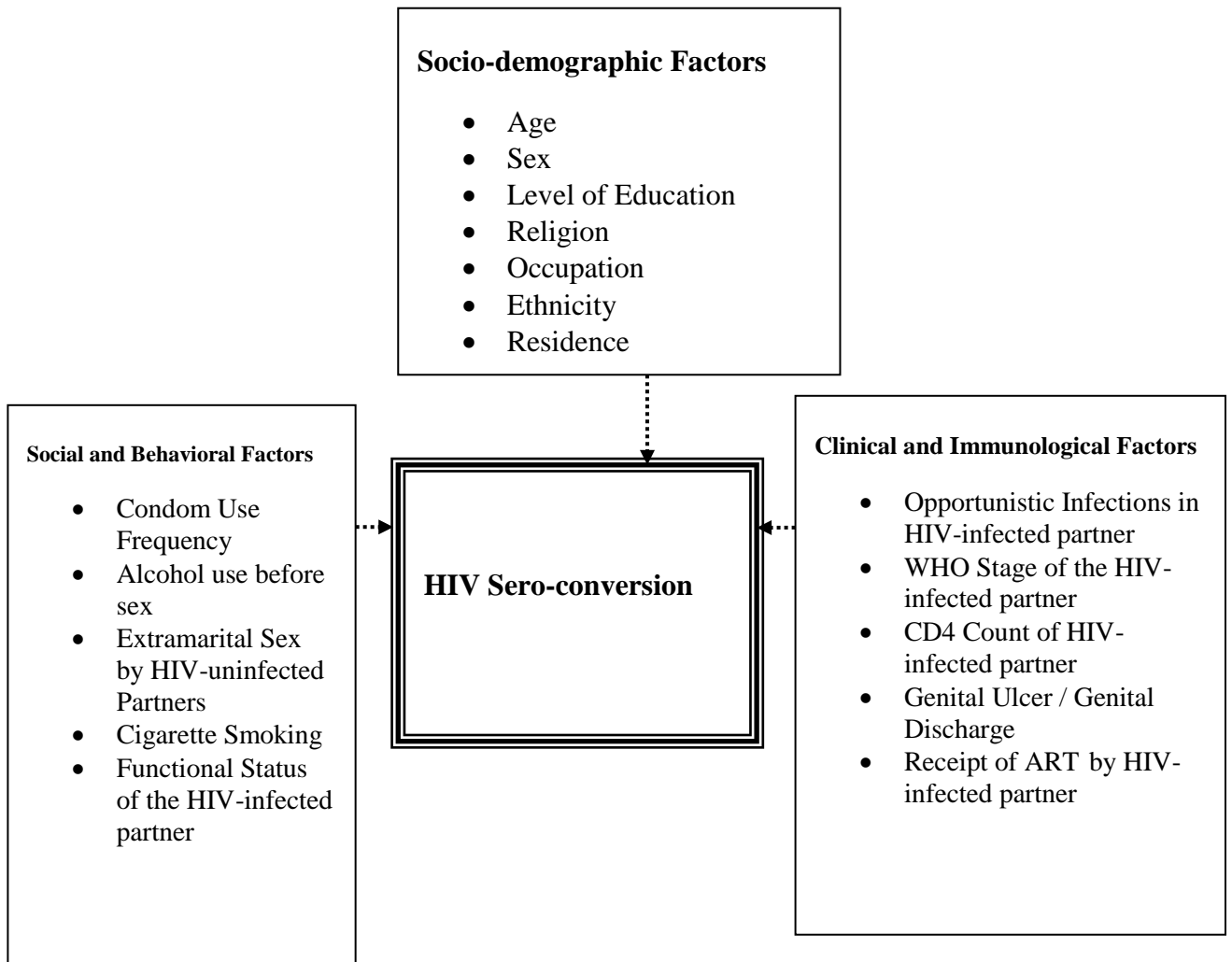
The magnitude of sero-discordance in Ethiopia and particularly in the study area is significant (2, 8). As the major mode of contracting the virus is heterosexual intercourse among couples with discordant serostatus, especially those negative partners within discordant partnership are the most vulnerable segment of the population to seroconvert.

Reported high incident of new infection among discordant couples presents unmet prevention need that has to be addressed quickly. Timely recognition of discordant couples or partners during Couples HIV-1 counseling and testing (CHCT) has valuable significance to curb the prevalence of this pandemic; as knowing their own or partner's serostatus and the options can motivate people to change higher risk behaviors. Moreover, knowing the magnitude and some determinants for sero-conversion rate would promote programs aimed at strengthening prevention of sexual transmission of HIV among Couples living in discordance.

Currently, there is no published data on sero-conversion rate and risk factors associated with acquisition of HIV in Discordant Couples in Ethiopia and in the study area. Having this research gap and significance in mind, it is worth and high time to get deployed in this particular study area.

Hence, this epidemiological study will be conducted on sero-conversion rate and identifying risk factors associated with acquisition of HIV in discordant couples. The findings will provide a basis for formulating strategies to strengthen programs of HIV prevention among discordant couples regionally and at the country level, which can be accomplished by adopting the WHO Guidance on Couples HIV Testing and Counseling and Antiretroviral Therapy for Treatment and Prevention in Sero-discordant Couples(4). This will consequently result into reduced incident of HIV arising from discordant couples.

**Figure 1:** A Conceptual framework for Predictors of HIV sero-conversion rate among discordant couples at JUSH.



## **Chapter Three: Objective**

### **3.1: General Objective:**

To determine Sero-conversion Rate and its Predictors among HIV Discordant Couples at JUSH, 2013.

### **3.2: Specific Objectives:**

1. To assess the socio-demographic characteristics of HIV-uninfected partners among HIV discordant couples at JUSH.
2. To assess the rate of sero-conversion among HIV Discordant Couples at JUSH.
3. To assess Predictors of sero-conversion among HIV Discordant Couples at JUSH.

## **Chapter Four: Methods**

### **4.1: Study Area and Period**

The study was conducted at ART clinic and VCT center of Jimma University Specialized Hospital (JUSH) from November 16/2013 to February 15/2014.

Jimma University Specialized Hospital is one of the teaching hospitals in the country located in Jimma town, Oromia region. The hospital serves as a referral hospital for southwestern Ethiopia including Jimma zone, which has a total population of 2,495,795 according to figures from the Central Statistical Agency in 2007(26).

The hospital is staffed with 1 medical resident,1 general practitioner,6 nurses, and a pharmacist who have trained in VCT service and management of people living with HIV.

Services at the ART clinic include integrated medical services for the treatment of HIV and related illnesses, prevention programs and nutrition counseling. All patients are treated according to Guidelines for Management of Opportunistic Infections and Anti Retroviral Treatment in Adolescents and Adults in Ethiopia 2008(27). Patients are seen every 3–6 months or as clinically indicated. At each visit the HIV-infected partners are advised for their partners to be screened for HIV.

In the VCT clinic the HIV-uninfected partner is followed every 3-6 months and screened for HIV. At the time of HIV VCT, each partner gives informed consent. All patients tested for HIV undergo pre and post-test counseling.

### **4.2: Study Design**

Retrospective cohort study was performed on sero-discordant couples in a single center.

### **4.3: Population**

#### **4.3.1: Source Population**

The source population was couples registered at the VCT center of JUSH and were tested for HIV.

#### **4.3.2: Study Population**

All sero-discordant couples (above 18 years old) among couples tested in JUSH VCT center that are selected from the registered clients in the period from 2003 to 2013 were included in the study according to the inclusion and exclusion criteria.

### **4.4: Inclusion and Exclusion Criteria**

#### **4.4.1: Inclusion Criteria**

The inclusion criteria required:

1. Appropriate written informed consent.
2. The couples remained together until six weeks to three months before the HIV-negative partner was screened for HIV for the last time in the follow up.

#### **4.4.2: Exclusion Criteria**

The participant was excluded if:

1. The couples who were separated six weeks to three months before the HIV-negative partner was screened for HIV
2. If the HIV-infected partner of the couples was lost to follow up after She/he was enrolled to the HIV chronic clinical care
3. If the HIV-infected partner died six weeks to three months before His/her partner was screened for HIV in the follow up
4. If the couples stopped sexual relations after they knew their status for HIV
5. If the couples were unwilling to participate in the study

## **4.5: Sample Size Calculation and Sampling Technique**

### **4.5.1: Sample Size**

All sero-discordant couples (above 18 years old) among couples tested in JUSH VCT center that are selected from the registered clients in the period from 2003 to 2013 were included in the study

### **4.5.2: Sampling Technique**

All participants attending the follow up clinic during the study period, and who fulfilled the inclusion criteria, were included.

## **4.6: Data Collection**

### **4.6.1: Data Collection Instruments and Data Collection Process**

Data was extracted from the registration book of the hospital and interviews using structured checklist specially designed for this study in English language.

The data collection process was as follows:

- Baseline data was collected for HIV-infected patients (index cases) including Clinical and Immunological Characteristics (i.e. Opportunistic infections, WHO stage and CD4 count), Social and Behavioral Characteristics (i.e. Condom use, Functional status) and about initiation of HAART after enrolment to care from data base of the registration book of the hospital.
- Data was collected for HIV-uninfected partner as follows :
  1. From the HIV-infected patients' (index cases) HIV Care/ART Card Family Form, if the partner was seroconverted and the ART Unique Number of the partner was documented, data was collected using this ART Unique Number of the seroconverter from the registration book of the hospital and was interviewed on his/her appointment day.
  2. On the follow-up visit date of the HIV-infected patient (index case), he/she was asked to come with his/her partner on the next visit day and to contact one of the data collectors. At this time invitation card was given and detailed locator information of the HIV-uninfected partner including telephone numbers for those who own or have access to a phone was collected.
  3. If the partners were absent on the appointment day or if the HIV-uninfected partner refused to come, he/she was contacted using his/her address.
  4. Finally, if the partners come together on the appointment day, for those partners who already seroconverted and were on follow-up, data was collected from the registration book using their ART unique number and those who reported that they are seronegative for HIV three months before, they were counseled and tested for HIV, the result and follow-up data were documented on the check list.
  5. If the data of the partners couldn't be assessed by the above measures the partners were taken as lost to follow-up.

#### **4.6.2: Data Collectors**

The data was collected by medical resident physicians working at the ART clinic of the hospital.

#### **4.6.3: Data Quality Control**

To ensure quality of the data the following measures were taken:

A three days training was given for data collectors before the start of data collection, the overall activities of data extraction was monitored by the principal investigator, and there was strict supervision during data collection, all completed data sheets were examined by the principal investigator for completeness during data collection, and consistencies of the collected data were checked during the analysis.

#### **4.7: Data Analysis**

All participants who completed at least one follow-up visit were eligible for statistical analysis. Person-years of observation (PYO) was calculated as the sum of the time from enrolment of HIV-infected (index) partner to the date of the last HIV-uninfected result, or to the estimated date of HIV infection for each participant. Date of HIV infection was imputed as the mid-point of the interval between the last HIV-uninfected and the first HIV-infected result dates. Statistical analyses was performed with SPSS version 16.0 computer software. Descriptive statistics was calculated with mean and standard deviation for variables that were normally distributed; and the median and interquartile range (IQR) were calculated for variables influenced by extreme values. Numbers (percentages) were used for categorical variables. Cox proportional-hazard modeling was used to assess the relationship between sero-conversion and potential risk factors. Univariate Cox models were used to assess the unadjusted relationship between sero-conversion and specified covariates of interest for all subjects. Covariates with a p-value <0.20 from the univariate analysis entered into a full multivariate Cox model to include significant covariates. The value of  $p < 0.05$  were considered statistically significant. Finally, analysis for risk data collected at the enrolment visit (baseline risk analysis) and data collected for follow-up visit (follow-up risk analysis) were performed.



## **4.8: Variables**

### **Dependent Variables**

HIV Status of HIV-uninfected Partners

### **Independent Variables**

- Socio-demographic Characteristics
- Opportunistic Infections in HIV-infected partner at enrollment and during follow-up
- WHO Stage of the HIV-infected partner at enrollment and during follow-up
- CD4 Count at enrollment and during follow-up period of the HIV-infected partner
- Condom Use frequency
- Functional Status of the HIV-infected partner during follow-up
- Alcohol Use before sex
- Cigarette Smoking
- Circumcision of HIV-uninfected male Partners
- Extramarital Sex in past 3 months by HIV-uninfected Partners
- Reported Genital Ulcer / Reported Genital Discharge
- Receipt of ART by HIV-infected partner at enrollment and during follow-up

## 4.9: Operational Definitions

1. **Discordant Couple:** is a couple where one partner is HIV positive, while the other is HIV negative. Couples were either married people or people cohabiting but not formally married, as reported by one of the couples and recorded on the charts.
2. **Condom Use** was categorized as :
  - (A) Always: use of condom during every sexual intercourse.
  - (B) Not always: includes one of the following :
    - Rarely: do use a condom whenever the patient thinks that the partner is a high-risk partner
    - Sometimes: use of condom for prevention of pregnancy;
    - Mostly: use of condom unless forgets;
    - Always: use of condom during every sexual intercourse or
    - Not asked
3. **HIV-Infected Partners** (index cases): one of the discordant who was HIV-positive and enrolled to the clinical care.
4. **HIV-Uninfected Partner:** one of the discordant who was HIV-negative during screening at VCT clinic with his/her partner for the first time.
5. **Sero-converter:** an individual who was HIV-uninfected partner and subsequently had a positive HIV test during follow-up.
6. **Non- sero-converter:** an individual who was HIV-uninfected partner and subsequently had a negative HIV test during follow-up.
7. **Person-years of Observation (PYO):** the sum of the time from enrolment of HIV-infected (index) partner to the date of the last HIV-uninfected result, or to the estimated date of HIV infection for each participant.
8. **Date of HIV infection:** the mid-point of the interval between the last HIV-uninfected and the first HIV-infected result dates.

#### **4.10: Ethical Considerations**

This study didn't involve any potentially harmful intervention to the patient and before official commencement of the data collection process, ethical clearance was obtained from the ethical committee of Jimma University. An official letter was obtained from the Department of Internal Medicine and was given to the responsible body at the ART clinic. Information obtained from the records were kept confidential by not recording the participant's name and the unique VCT code number on the questionnaires; instead new code numbers were given by the principal investigator and later after data entry, the code numbers were permanently destroyed. Couples were given the informed consent document to read or, if illiterate, it was read to them by a data collector in the presence of an independent witness.

#### **4.11: Dissemination of Results**

The findings of this study will be given to the department of Internal Medicine. Thereafter, it will be disseminated to non-governmental stake holders working in the area through presentations on conferences. Further effort will be made to publish in peer- reviewed national and international journals..

## Chapter Five: Result

### Enrolment, Baseline Characteristics and Retention

During the study period of four month, from November 16/2013 to February 15/2014, a total of 194 discordant couples were screened for eligibility and the HIV-uninfected partner was enrolled into the study. Of these 67 couples (34.5%) were HIV discordant but the HIV-uninfected partner did not meet one or more of the other eligibility criteria:24 due to couple separation,10 lost to follow-up,12 death of HIV-infected partner, 13 were unwilling in the study, and 8 stopped sexual relation with partner. Finally a total of 117 HIV-uninfected partners were included in the study.

### Incidence of HIV among HIV discordant couples

Out of 117 HIV-uninfected partners,11(9.4%) participants seroconverted over a total of 652.7 PYO(mean=5.6). The overall HIV incidence rate was 1.7; and 1.8 and 1.6 per 100 PYO in men and women, respectively (Table 1).

**Table 1: The rate of sero-conversion among HIV discordant couples at ART clinic**

Variabes	Total N (%)	Seroconverters N (%)	Non-sero- converters N (%)	PYO	Rate/ 100 PYO
Male	71(100)	7(9.9)	64(90.1)	399.9	1.8
Female	46(100)	4(8.7)	42(91.3)	252.8	1.6
Total	117(100)	11(9.4)	106(90.6)	652.7	1.7

## The Socio-Demographic Characteristics of HIV-Uninfected Partners

The socio-demographic characteristics of the patients are depicted in Table 2. In general, the mean age of the study participants was 36.5 years (standard deviation, SD: 9.9), most (65.2%) were male and 34.8 were female. Of 11 seroconverters, 8(72.7%) of them belong to the age group of 50 years old and above, 3(27.3%) belong to the age group 25-34. Concerning religion, 9 (81.8%) and 2 (18.2%) of orthodox Christians and Muslims, respectively, were seroconverted. Regarding the level of education, among 83 couples who have formal education, 7(8.4%) seroconverted. Of 34 couples, who had no formal education, 4(11.8%) of them seroconverted. At univariate analysis, there was no association between the socio-demographic variables with risk of seroconversion.

**Table 2: Socio-demographic characteristics of the HIV-uninfected partners**

Variables	Total N (%)	Seroconverters N (%)	Non-seroconverters N (%)	RR (95% CI)	p-value
<b>Sex</b>					
Male	71(100)	7(9.9)	64(90.1)		0.93
Female	46(100)	4(8.7)	42(91.3)		
<b>Age</b>					
≥ 35	68(100)	8(11.8)	60(88.2)		0.80
25-34	46(100)	3(6.5)	43(93.5)		
18-24	3(100)	0(0)	3(100)		
<b>Level of Education</b>					
Formal education	83 (100)	7 (8.4)	76 (91.6)		0.76
No formal education	34 (100)	4 (11.8)	30 (88.2)		
<b>Religion</b>					
Muslim	34(100)	2 (5.9)	32 (94.1)		0.74
Orthodox	64 (100)	9 (14.1)	55 (85.9)		
Protestant	19 (100)	0 (0)	19 (100)		
<b>Occupation</b>					
Unemployed	57(100)	6(10.5)	51(89.5)		0.59
Farmer	3(100)	0(0)	3(100)		
Employed (paid work)	56(100)	5(8.9)	51(91.1)		
Student	1(100)	0(0)	1(100)		
<b>Ethnicity</b>					
Oromo	56(100)	6(10.7)	50(89.3)		0.67
Amhara	23(100)	3(13)	20(87)		
Tigre	7(100)	0(0)	7(100)		
Others	31(100)	2(6.5)	29(93.5)		
<b>Residence</b>					
Urban	112(100)	11(9.8)	101(90.2)		0.56
Rural	5(100)	0(0)	5(100)		

### Characteristics of HIV-uninfected Partners

Crude associations between characteristics of HIV-uninfected partners and HIV acquisition are presented in Table 3. Regarding condom use behavior of HIV-uninfected partners, no seroconversion occurred among participants who reported always using condoms during the study period. Among 27 HIV-uninfected partners who used alcohol before sex, 3(11.1%) and of 90 who didn't use alcohol, 8(8.9%) of them seroconverted. Of 2 partners who experienced and 115 who didn't experienced extramarital sex in past 3 months, none and 11(9.6%) of them, respectively, seroconverted in the study period. There was no association between alcohol use before sex and extramarital sex in past 3 months with risk of seroconversion. None of HIV-uninfected partners had history of reported genital discharge or genital ulcer in the study period.

**Table 3: Characteristics of HIV-uninfected Index Partners**

Variables	Total N (%)	Sero-converters N (%)	Non-sero- convertersN (%)	RR (95% CI)	p- value
<b>Condom use frequency</b>					
Always	77(100)	0 (0)	77 (100)	-	-
Not always	40(100)	11(27.5)	29(72.5)		
<b>Alcohol use before sex</b>					
Yes	27(100)	3(11.1)	24(88.9)		0.94
No	90(100)	8(8.9)	82(91.1)		
<b>Cigarette smoking</b>					
Yes	12(100)	1(8.3)	11(91.7)		0.86
No	105(100)	10(9.5)	95(90.5)		
<b>Extramarital sex in past 3 months</b>					
Yes	2(100)	0(0)	2(100)		0.67
No	115(100)	11(9.6)	104(90.4)		

### Characteristics of HIV-infected Index Partners

Crude associations between Characteristics of HIV-infected index partners and HIV acquisition are presented in Table 4. A total of 13 HIV-uninfected partners had HIV-infected partners who were found to have persistent generalized lymphadenopathy (PGL) of which 4(30.8%) seroconverted, while 9(69.2%) didn't seroconvert and among 20 HIV-uninfected partners who had HIV-infected partners with a past history of herpes infection, 3(15%) of them seroconverted and 17(85%) didn't. On the other hand, among the 35 HIV-uninfected partners who had HIV-infected partners with oral candidiasis at enrollment, only 1(7.1%) of them seroconverted and 13(92.9%) didn't. At univariate analysis, there was no association between these opportunistic infections and risk of seroconversion. Regarding the WHO clinical stage of the HIV-positive patient at enrollment and the serostatus of the HIV-uninfected partner, among 19 HIV-uninfected partners whose partners were in WHO clinical stage I, 34 in stage II, 51 in stage III and 13 in stage IV: 6(31.6%), 4(11.8%), 1(2%) and none, respectively, seroconverted in the study period. HIV-uninfected partners whose partners were in WHO clinical stage II and III were less likely to seroconvert [RR(95% CI) =0.2 (0.06-0.83) and 0.03(0.04-0.27), respectively]. No seroconversion occurred in HIV-uninfected partners whose partners were in WHO clinical stage IV.

Regarding CD4 count at enrollment, among 63 HIV-uninfected partners whose partner's CD4 count at enrollment(cells/mm<sup>3</sup>) was less than 200, 3(4.8%) of them seroconverted and of 54 HIV-uninfected partners whose partner's CD4 count at enrollment(cells/mm<sup>3</sup>) was 200 and above, 8(14.8%) of them seroconverted. There was no association between the CD4 count at enrollment and risk of seroconversion.

Among 79 HIV-uninfected partners whose partners receive ART at enrollment, 5(6.3%) of them seroconverted and 74(93.7%) didn't seroconvert. Regarding functional status during follow-up, 110 of HIV-infected partners were working, 5 ambulating and 2 of them bedridden and only 11(10%) of HIV-uninfected partners whose partners were working, seroconverted in the study period. There was no association between Receipt of ART at enrollment and functional status during follow-up with risk of seroconversion. None of HIV-infected partners had history of reported genital discharge or genital ulcer in the study period.

Table 4: Characteristics of HIV-Infected Index partners

Variables	Total N(%)	Seroconverters N (%)	Nonseroconverters N (%)	RR (95% CI)	p- value
<b>Opportunistic infections at enrollment</b>					
PGL	13(100)	4(30.8)	9(69.2)		0.36
Herpes zoster	20(100)	3(15)	17(85)		
Oral candidiasis	14(100)	1(7.1)	13(92.9)		
<b>WHO stage at enrollment</b>					
Stage I	19(100)	6(31.6)	13(68.4)	1	0.006
Stage II	34(100)	4(11.8)	30(88.2)	0.2 (0.06-0.83)	
Stage III	51(100)	1(2)	50(98)	0.03(0.04-0.27)	
Stage IV	13(100)	0(0)	13(100)	0	
<b>CD4 count at enrollment(cells/mm3)</b>					
<200	63(100)	3(4.8)	60(95.2)		0.09
≥200	54(100)	8(14.8)	46(85.2)		
<b>Receipt of ART at enrollment</b>					
Yes	79(100)	5(6.3)	74(93.7)		0.09
No	36(100)	6(15.8)	32(84.2)		
<b>Functional Status during follow-up</b>					
Working	110(100)	11(10)	99(90)		0.74
Ambulating	5 (100)	0 (0)	5 (100)		
Bedridden	2 (100)	0 (0)	2 (100)		
<b>Alcohol use before sex during follow-up</b>					
Yes	6 (100)	0 (0)	6 (100)		0.45
No	111 (100)	11 (9.9)	100(90.1)		
<b>Cigarette smoking during follow-up</b>					
Yes	5(100)	1(20)	4(80)		0.32
No	112(100)	10(8.9)	102(91.1)		



## Predictors of Sero-conversion among HIV Discordant Couples

Factor that remained significantly associated with increased risk of HIV acquisition at multivariate analysis was WHO stage at enrollment. HIV-uninfected partners whose partners were in WHO clinical stage II and III were less likely to seroconvert [RR(95% CI) =0.2 (0.06-0.83) and 0.03(0.04-0.27), respectively] as compared with those in WHO stage I. No seroconversion occurred in HIV-uninfected partners whose partners were in WHO clinical stage IV.

Table 5: Predictors of Sero-conversion among HIV Discordant Couples

Variables	Total N (%)	Seroconverters N (%)	Nonseroconverters N (%)	RR (95% CI)	aRR (95% CI)
<b>Condom use frequency</b>					
Always	77(100)	0 (0)	77 (100)	-	-
Not always	40(100)	11(27.5)	29(72.5)		
<b>WHO stage at enrollment</b>					
Stage I	19(100)	6(31.6)	13(68.4)	1	0.006
Stage II	34(100)	4(11.8)	30(88.2)	0.2 (0.06-0.83)	
Stage III	51(100)	1(2)	50(98)	0.03(0.04-0.27)	
Stage IV	13(100)	0(0)	13(100)	0	

## Chapter Six: Discussion

This study is the first retrospective cohort study on serodiscordant couples in a Jimma university specialized hospital with the objective of determining the seroconversion rate and predictors for HIV acquisition.

With the study period of 4 months, a total of 194 discordant couples were in the follow-up clinic and screened for eligibility, of these 117 HIV-uninfected partners who met the eligibility criteria were included in the study.

The overall HIV incidence in this cohort was 1.7 per 100 PYO that was lower than the rates reported in previous HIV discordant couple studies in Masaka, Uganda (14). In this study only one third of patients started ART. Almost 72% of the HIV-infected partners of our participants had initiated ART at enrollment. This may help to explain the lower HIV incidence in our cohort compared to the previous study. However the incidence rate is almost comparable with the other studies done in south Zhumadian city, Henan province, China which was 1.71 per 100 PYO(12).

We found no significant difference in HIV incidence between men and women, the rate being about 1.8 and 1.6 per 100 PYO for each gender respectively. Recent studies in Rakai and Masaka found similar HIV transmission risks among men and women(14, 16).

We found that regular condom use was strongly protective against HIV acquisition. Among participants, who reported always using condoms, none of HIV-uninfected partners seroconverted. This was similar with other literatures included in the review(19) and analyses from the Partners in Prevention HSV/HIV Transmission Study found that male condoms were associated with 79% lower risk of HIV-1 transmission (24).

In our study, HIV-uninfected partners whose partners were in WHO clinical stage II and above were less likely to seroconvert as compared with those in WHO stage I. In a retrospective population-based cohort study done on 235 monogamous, HIV-discordant couples in Ugandan, after seroconversion of the index partner, the rate of transmission within the first 2.5 months was almost 12-fold higher than that observed in prevalent index couples (19). This high likelihood of HIV transmission in early stages of HIV was explained primarily in accordance with relatively high plasma viral load.

## **Chapter Seven: Limitations of the study**

Improper documentation of the couples address, date confirmed HIV positive and related important variables in the index partner's registration card in the ART clinic affected the tendency to trace the partners and enroll in the study.

Inconsistent follow-up of HIV-discordant couples regularly in JUSH VCT center, that resulted in loss from follow up.

## **Chapter Eight: Conclusion**

Our study found a low rate of HIV transmission among serodiscordant couples in the study area. Late WHO stage at enrollment was predictive of a reduced risk of HIV acquisition. In addition the study has shown that correct and consistent use of condoms is a highly effective tool for HIV-1 prevention (no seroconversions occurred among participants who reported always using condoms during the study period).

## **Chapter Nine: Recommendations**

Our study found a low rate of HIV transmission among serodiscordant couples in the study area, but it contributes to a clinically significant population that mandates implementation of preventive strategy. The finding that no seroconversion occurred among participants who always use condom in our study shows consistent condom use is strongly protective of HIV acquisition and this practice should be strengthened and continued in the study area. Further studies are needed to see the incidence in different regions of the country. Finally, the reduced risk of HIV acquisition among participants whose partners were at late WHO stage at enrollment in this study points a need for further study to ascertain this association.

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## **Annexes I: Questionnaires**

Data collection instrument on sero-conversion rate and factors associated with acquisition of HIV in discordant couples at JUSH, ART clinic.

### **Part I: To be filled for all HIV-uninfected partners**

Research code number \_\_\_\_\_

#### **A: Questions on HIV status of the HIV-uninfected partner:**

1. When was the last time he/she was screened for HIV? \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ (dd/mm/yr)
2. What was the result? a. HIV positive b. HIV negative

#### **B: Questions on Socio-demographic feature of the HIV-uninfected partner:**

1. Age \_\_\_\_\_ Yrs
2. Sex a. Male b. Female  
If male: a. Circumcised b. Uncircumcised
3. Level of education a. Illiterate b. Able to read and write only c. Formal education
4. Religion a. Muslim b. Orthodox c. Protestant
5. Occupation a. Unemployed b. Farmer c. Employed (paid work) d. Student
6. Ethnicity a. Oromo b. Amhara c. Tigre d. Others(specify)\_\_\_\_\_
7. Residence a. Urban b. Rural
8. Address Zone \_\_\_\_\_  
Woreda \_\_\_\_\_  
Kebele \_\_\_\_\_  
House number \_\_\_\_\_  
Phone number (Mobile or Home) \_\_\_\_\_



**C: Questions on Clinical and Immunological characteristics of HIV-infected index partners during follow-up period:**

1. Opportunistic Infections? a. PGL b. TB c. Herpes zoster  
d. Oral candidiasis e. Others \_\_\_\_\_
2. The last recorded CD4 count (cells/mm<sup>3</sup>) during follow-up \_\_\_\_\_
3. WHO stage during follow-up \_\_\_\_\_
4. Receipt of ART during follow-up? a. Yes b. No
5. Reported Genital Ulcer? a. Yes b. No
6. Reported Genital Discharge (for female)? a. Yes b. No
7. Status after the last follow up time 1. Active 2. Dead 3. Lost 4. Dropped  
5 . Transferred out 6. Other (specify) \_\_\_\_\_

**Annexes II: Informed Consent Form**

**A) Information to the Participant**

Date .....

Good Morning / Afternoon.

I am.....a physician working in JUSH. We are conducting a research on Sero-conversion Rate and Its Predictors among HIV Discordant Couples at Jimma University Specialized Hospital ART clinic. If you are willing, we want to involve you in the study and all we do is ask you some health related questions. Your participation is entirely based on your willingness and your refusal doesn't affect the service you get from us in any way.

The information obtained from the interview, the measurements and your examination results will be kept confidential and will be used for the stated objectives only.

**B) Certificate of Consent (English)**

Do you wish to participate in the study?

If the participant agrees to participate in the study, proceed with interview after the patient has signed the consent.

I have adequate information about the research and I have decided to participate in the study.

Signature \_\_\_\_\_

If the participant says "No, I don't want to participate in the study", thank him (her) and stop.

Thank you!

Name of interviewer \_\_\_\_\_

Date \_\_\_\_/\_\_\_\_/\_\_\_\_

C) Certificate of Consent (Amharic)

**፩ ለተሳታፊው የሚሰጥ የጥናት ውል ማስገንዘብያ**

እኔ ዶ/ር ኤልያስ ጉልማ የተባልኩ የውስጥ ደዌ ህክምና ት/ት ክፍል የመጨረሻ አመት ሬዚደንት የመመረቂያ ፀ-ሁፊን ለመስራት ለሚያስፈልገኝ ጥናት እርስዎ መመረጥዎን ሳሳውቅዎት በታላቅ ስታ ነው።

ጥናቱ የሚካሄደው በቃል መጠይቅ ሲሆን እርሶም ፈቃደኛ ከሆኑ የተወሰኑ ጥያቄዎች በመመለስ ተሳታፊ እንዲሆኑ እንጠይቃለን። የሚሰጡን” መረጃ በሚሰጥር የምንጠብቀው ሲሆን የርሶ ስምና ሊሎች የርሶን ማንነት የሚያመለክቱ ነገሮች በጥናቱ ላይ አይገቡም።

ከጥናቱ መውጣት ከፈለጉ በማንኛውም ሰዓት አቋርጠው መውጣት ይችላሉ። ይህም በማድረግዎ ምንም ተጽህኖ አይደርስብዎትም፤ በሚያገኙት የህክምና አግልግሎት ላይም ተጽኖ የለውም።

ከጥናቱ የሚገኘው ውጤት ወደፊት የሚካሄዱ ሌሎች ጥናቶች መነሻ ከመሆኑም ባሻገር የተፈለገው ጥናት በዞናችን ምን እንደሚመስል ያስገነዝባል።

አመሰግናለሁ።

**፪ ተሳታኝ  አቃ ኝነት ማረጋገጫ ቅፅ**

ስለጥናቱ በቂ እውቀት ስላገኘሁ በሙሉ ፍቃደኝነት ለመሳተፍ ወስኛለሁ።

ተሳታኝ ኝርም \_\_\_\_\_

ተሳታፊው በጥናቱ ለመሳተፍ ካልፈለገ አመስግነው ያሰናብቷቸው።

የጥናቱ አስተባባሪ ፊርማ \_\_\_\_\_

ቀን \_\_\_ / \_\_\_ / \_\_\_

## C) Certificate of Consent ( Afaan Oromotin)

### 1. Oddeffanoo Qoratamaaf kenamu

Ani maqaan koo Dr Elias Gullma yoon ta’u, Karoora barrefama eebbaa irrati hirmaataa akka naaf taatan kabajaan isin gaafadha. Qorannoon kun kan adeemsiifamu bifa gaaffiifi qorannoo dhiigatiin yoo ta’u , rakkoon tokkoyuu isin irran hin gahu.Qorrannoon kun saatii tokko caala hinfudhatu.Ooddeffanoon qorrannoo kanarraa argamu hoojjii fundurraaf adeemsamuuf gargaarsa guddaa kenna. Qorrannoo keessaa yeroo barbaadaniti bahuun kan danda’amu yoo ta’u, kuni immo tajaajila isiinii keennamu irrati dhiibbaa hoommayyu hin qabu.

### 2. Mallattoo Mirkanessaa

Qo’anna irrati qooda fudhachuuf yoo waligaltan bakka armaan gaddii irrati mallatton mirkenessa.

Galatoomaa

Mallattoo \_\_\_\_\_

Maqaa –Qorrata goodhuu \_\_\_\_\_

Guyyaa \_\_\_\_\_

Yoo qo’anna irrati qooda fudachuu hin barbaadne taanan,Isaan geleteessaati dhiisaa.

**Annexes III: Ethical Clearance Request Form**

Date.....

To Jimma University Ethical Review Committee.

Subject: Request for Ethical Clearance.

I am a final year medical resident preparing to conduct a research entitled Sero-conversion Rate and Its Predictors among HIV Discordant Couples at Jimma University Specialized Hospital ART clinic

This is the first research of its kind to be conducted in this setup and I hope it will give a clue about the magnitude of the problem and will serve as an entry point for further related researches.

I hereby request the committee to revise the proposal and grant me an ethical clearance to proceed with the research process.

With Regards

**ELIAS GULLMA (MD)**

(Principal Investigator)

Name and Signature of Advisors

**1. Dr. Ermias Habte (Internist)** \_\_\_\_\_

**2. Dr. Daniel Yilma (Internist)** \_\_\_\_\_

**3. Mr. Dessalegn Massa (BSc, MPH)** \_\_\_\_\_